American Journal of Hematology 52:224–226 (1996)

Aberrant CD2 Expression in Precursor-B Acute Lymphoblastic Leukemia of Childhood

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Aberrant CD2 expression in childhood precursor-B ALL is rare and has recently been reported with an incidence of 3.6% in a study by Cantu-Rajnoldi et al. [*Haematologica* 77:384, 1992]. There was no association of the CD2 co-expression with other known prognostic factors. Our study represents the second one in the literature. Out of 60 childhood acute lymphoblastic leukemias, analyzed morphologically and by flow cytometric immunophenotyping, 49 were of precursor B origin. Of these 49 cases, CD2 co-expression was detected in 2, yielding an incidence of 4.1%. The complete immunophenotypic profiles of these two cases were as follows, respectively: (1) CD19+, CD20−, CD24+, CD10+, sIg−, CD2+, CD3−, CD5−, CD7−, CD13−, CD33−, CD34+, Tdt+; and (2) CD19+, CD20−, CD24+, CD10+, sIg−, CD2+, CD3−, CD5−, CD7−, CD13+, CD33−, CD34+, Tdt+. Cytogenetic analysis revealed a normal male chromosome pattern in case 1 and an abnormal female chromosome pattern [4 cells: 46, XX, del (6q) (q21 q23) and 9 cells: 46, XX, del (11q) (q14 q23)] in case 2. Both patients were in continuous complete remission at last follow-up. © 1996 Wiley-Liss, Inc.

Key words: precursor-B acute lymphoblastic leukemia, CD2 expression, flow cytometric analysis

INTRODUCTION

CD2-positivity(+) in precursor-B acute lymphoblastic leukemia (PBALL) has rarely been reported; the first two cases were reported by Ludwig et al. [1] and Bradstock et al. [2]. The first study analyzing CD2+/CD19+ in adult/childhood ALL revealed an incidence of 1.5% (5/336) [3]. All 5 cases were childhood CD10+, CD34+ pre-pre-B ALL and attained initial complete remission (CR); 4 maintained complete continuous remission (CCR), 3–4 years follow-up and 1 relapsed, with CR 3 years post-reinduction.

There is only one study reporting the incidence of CD2+/E-rosette+(E+) childhood precursor-B ALL (CPBALL) [4]. In that study 3.6% (11/306) showed CD2+(9 cases)/E+(2 cases) in otherwise typical common ALL (L1 morphology); 2/11 had a white blood cell (WBC) count $>20 \times 10^9$/L; 7/11, $\leq 4.6 \times 10^9$/L and none had a radiographic mediastinal mass. CR was obtained in all cases. Three out of eleven patients relapsed, 2/3 died of progressive disease, and 1/3 was in therapy at last follow-up. Eight out of eleven (73%) maintained CCR (36–93 months). Neither study reported cytogenetic data.

Since the incidence of CD2+CPBALL has only recently been reported once, we report our incidence of CD2+ in 49 cases of CPBALL, defined by morphology and flow cytometric immunophenotyping (FCI).

MATERIALS AND METHODS

Morphologic/Flow Cytometric Analysis

Sixty peripheral bloods or bone marrow aspirates with ≥60% "lymphoblasts" morphologically were consecutively analyzed for various antigens using a FACSCAN flow cytometer (Becton-Dickinson, Mountainview, CA), standard techniques, and commercially available monoclonal antibodies, including CD1, CD15, HLA-DR (Ortho-Diagnostic Systems, Raritan, NJ); CD2, CD10, CD13, CD14, CD19, CD20, CD33, CD56 (Coulter Clone, Coulter Immunology, Hialeah, FL); CD3, CD4, CD7, CD45 (Becton-Dickinson, San Jose, CA); CD5, CD8

Received for publication February 20, 1996; accepted March 6, 1996.

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TABLE I. Clinical, Hematological, Flow Cytometric Immunophenotypic (FCI) Data

Clinical/hematological data			FCI data[a]		
	Case 1	Case 2		Case 1	Case 2
Age (years)	2.5	13	CD19	66	93
Hgb (g/dl)	6.6	11.6	CD20	1	11
WBC ($\times 10^9$/L)	4.6	30.8	CD24	74	80
PLTS ($\times 10^9$/L)	91	242	CD10	29	49
Mediastinal mass	—	—	SIg	4	3
Therapy	Low-risk	High-risk[b]	CD2	76	81
Clinical outcome	CCR[c]	CCR	CD3	18	4
Survival (months)	24	23	CD5	17	4
			CD7	17	4
			CD13	10	42
			CD33	15	1
			CD34	66	93

[a]All results given as percent positive cells in bone marrow.
[b]High-risk, due to age and WBC count.
[c]CCR, complete continuous remission.

(Gen Trak, Inc., Wayne, PA); CD24 (Hybritech, Inc., San Diego, CA); CD34 (Gen Trak, Plymouth Meeting, PA); C-Kit (AMAC, Inc., Westbrook, ME); and IgA, IgD, IgG, IgM, Kappa, Lambda (Kallestad, Inc., Chaska, MN). Antigen "positivity" meant >20% of cells reacted with the antibody. Forty-nine out of sixty were PBALL (CD19+, CD24+, CD20+, CD10+, SIg−), 11/60 failed the criteria or were T-ALL. Pre-pre B was defined as CD19+, CD24+, CD20−; Pre-B, CD19+, CD24+, CD20+ [5]. "Aberrant" expression meant the sum of the percentage of cells positive (PCP) for the particular marker plus the PCP for the most reliable lineage marker (i.e., CD10, CD19, or CD24 in PBALL) was ≥120%.

Terminal deoxynucleotidyl transferase (TdT) was performed by standard immunofluorescent technique using mouse anti-human TdT mixture (Supertechs, Inc., Biotechnology Consultants, Bethesda, MD) and Dialux-20 fluorescent microscope (Leitz, Rockleigh, New Jersey).

RESULTS

Flow Cytometric/Morphologic Findings

Of the 49 cases of PBALL, the majority (67%) was of pre-pre B origin, CD10+; 16%, pre-B origin, CD10+; 12%, pre-pre B origin, CD10−; and 4% were classified as of precursor B origin, CD10−, since CD20 was not performed in these cases. The 2/40 (4.1%) with CD2+ were of pre-pre B origin, CD10+, CD34+ with L2 morphology. One case had aberrant CD13+ (Table I). TdT was positive (≥60%) in all cases.

Clinical Correlations

Table I shows clinical/hematological data for the two CD2+CPBALL. Both patients had minimal signs and symptoms; case 1, epistaxis only; case 2, cervical lymphadenopathy only. Bone marrow cytogenetic results revealed a normal male chromosome pattern (case 1) and an abnormal female chromosome analysis (case 2) [4 cells: 46, XX, del (6q) (q21 q23); 9 cells: 46, XX, del (11q) (q14 q23)].

DISCUSSION

CD2+/E+ in B cell malignancies has rarely been described. Guglielmi et al. described 3 patients with E+B-cell chronic lymphocytic leukemia [6]. These E+B-cells lacked detectable T cell antigens.

CPBALL may rarely be associated with CD2+; there are 17 such reported cases [1–4]. The incidence of CD2+ in the only study of CPBALL is 3.6% [4]; no clinical significance was identified.

Our study represents the second one analyzing the incidence of CD2+CPBALL. We found 4.1% (2.49) showed CD2+pre-pre BALL with CD10+, CD34+, and L2 morphology. One case had aberrant CD13+. Both patients, with minimal symptomatology, achieved CCR within 1 month of therapy; last follow-up was 24 and 23 months, respectively. The abnormal chromosomal analysis (case 2) did not necessarily indicate a worst prognosis. Good prognostic indicators included a CD10+, CD34+ pre-pre B immunophenotype. The significance of aberrant CD13+ in case 1 is controversial. L2 morphology, as in our patients, indicates a less favorable outcome than L1 morphology [7]. Our case number is too small for prognostic conclusions.

CD2+ in PBALL has been postulated to arise from a small population of fetal liver and bone marrow lymphoid cells with CD2+/CD19+ [21]. However, these cells lack CD13 and this postulate would not explain the existence of CD2+, CD13+PBALL. Aberrant gene regulation in leukemic cells may explain the unusual co-expression of

antigens with specificity for different hemopoietic cell lineages in these cases [8]. Unusual co-expression of antigens may also imply that there are only a few antigenic determinants entirely restricted to a particular cell lineage [9]. In our opinion, aberrant CD2+ in CPBALL represents lineage infidelity. Future genotyping of cases may support this view.

ACKNOWLEDGMENTS

The authors acknowledge Rosemary Baxter and Patty Jenkins for secretarial assistance and Jesse Urhahn for photographic assistance.

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